

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Evaluation of electronic prescription implementation in polymedicated users of Catalonia, Spain: a population-based longitudinal study
AUTHORS	Mariño, Eduardo; Lizano-Díez, Irene; Modamio, Pilar; López-Calahorra, Pilar; Lastra, Cecilia; Segú, Luis; Gilabert-Perramon, Antoni

VERSION 1 - REVIEW

REVIEWER	Carlos Campillo-Artero Balearic Health Service, Palma de Mallorca, Spain
REVIEW RETURNED	31-Jul-2014

GENERAL COMMENTS	<p>This is an interesting piece of work that should be welcomed since it is an example of the usefulness that information provided by the evaluations of health services interventions entail with regard to policy making, a health services and policy research goal that has long been called forth in many countries. Having this said notwithstanding the paper should be reviewed in depth before considering its suitability for publication.</p> <p>My main concerns are fifthfold.</p> <p>First, the objective should be reviewed. Strictly speaking, "to analyse drug use indicators..." is not an objective but a methodological step aimed at an end. One analyses indicators in the pursuit of one purpose. This purpose is likely to be the objective. Moreover, in cases such as this one, both process and outcome indicators are what readers and policy makers are interested the most. In this study only process indicators are used. It is worth remembering that what is really at issue and what the study is eventually revolving around is a causal relationship between Rec@t and "process" along with health improvement.</p> <p>Second, despite the authors recognize some of the limitations of their research, they do not do so explicitly. I would recommend including some paragraphs explicitly devoted to them in the Discussion. Two of these limitations are paramount. First, there is no control group (what indisputably limits internal validity and undoubtedly impedes establishing causal relationships between Rec@t and both process and outcome indicators). Second, as the authors state, the period covered by the study is too short a time to establish these relationships with a reasonable degree of uncertainty, and the implementation of the program is still limited should they actually pursue a complete process and outcome evaluation of the intervention.</p> <p>Third, the assessment was limited to 6 BHAs. This limitation should</p>
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	<p>be added to the former in order to fully ascertain the full contribution of this paper.</p> <p>Fourth, this study is not cross-sectional. It is longitudinal and includes a non-concurrent and a concurrent phase. The authors indicate that it is also descriptive and exploratory. Since this seems to be known ex ante it also precludes from drawing causal associations between Rec@t and the results.</p> <p>Fifth, sources of variability of the results are clearly recognized in the Discussion, a fact that further calls for caution before drawing conclusions concerning the “quality, accessibility, safety, efficiency, continuity of care, rational use of drugs”, some of the main features that should be eventually improved with the implementation of a program such as Rec@t. All of them are legitimate goals of the program, but this study does not allow to ascertain to what extent they have been fulfilled.</p> <p>The study provides a very valuable but initial and partial approach for current managerial, control and follow-up purposes. It is not appropriate though for assessing either the effectiveness, the efficiency or the future impact assessment, given the abovementioned reasons. Both the time elapsed since its inception and its degree of implementation explain among other reasons that the study still falls short of doing so.</p>
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REVIEWER	Hannes Enlund Finnish Medicines Agency, Finland
REVIEW RETURNED	13-Aug-2014

GENERAL COMMENTS	<p>The increase in costs of pharmaceuticals in different national health service systems has resulted in the need to monitor these costs and assess the effects of different cost containment measures. The manuscript describes efforts in the Catalan Health Service to monitor prescribing in general population and among polymedicated patients using different indicators. Of special interest is the effects of the new e-prescribing system.</p> <p>The manuscript has some merits, but needs to be clarified on certain points especially to an international audience not familiar with the Spanish and Catalan health care system.</p> <p>The introduction is basically a description of the background and Catalan health care and the introduction of a new electronic prescription system. The introduction would improve with a more thorough presentation of the available literature (or lack of it) from an international point of view, especially when the authors have done a systematic literature search. Some of the current system description could rather be included in the methods section as “Setting” than in the introduction.</p> <p>The introduction has a paragraph on the aims of the study. This could be reformulated to better reflect the aims, e.g. which drug use indicators and why the study was done or for what purpose the findings will be used. Is the main aim to study the deployment of the e-prescribing or the “effects” in polymedicated patients?</p> <p>The method states that study is interventional, but the discussion states that the study is an exploratory, descriptive and transversal study. This makes the reader somewhat confused as the results is</p>
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	<p>based on a 16 retrospective and 12 month prospective follow-up. It would be helpful to give the rationale for using 16 drugs as the cutoff point for “polymedicated” patient since this is not used by other authors.</p> <p>The polynomial modeling that is used in the figures and appendices I would recommend leaving out. In this case the value of higher order equations is questionable in predicting future trends. Rather analyze the trends of time series for period 1 (before) and period 2 (after) and possible interactions.</p> <p>For an international audience some additional information would be helpful for better understanding of the setting and system. For example for a how long time period is a prescription usually issued in chronic diseases, one month, three months or a year? What is the average number of prescriptions per capita/year or month in Catalan or Barcelona health region and also cost per prescription. I had also problems in trying to understand whether the same person can be a polymedicated patient in different points of the follow-up and what the consequences are for the analysis. Is there a real increase in polymedicated patients (new polymedicated or the same patients as before?). Is the analysis based on prescriptions or individuals counted only once during the follow-up?</p> <p>The results section would improve by inserting subheadings on the deployment in general population and on the other hand results related to “polymedicated” patients.</p> <p>On page 6 line 10 says “only 6 reached the highest cumulative implementation grade...” rather say “only 6 reached a 25% implementation grade. Then the next sentence can be deleted.</p> <p>In Table 1 insert a column on average number of prescriptions/user in the different BHAs (i.e. $438,228/107,306=4.1$ etc.)</p> <p>Table 2 says “number of polymedicated users” but there is no such number included! It is also unclear whether average number of prescriptions per polymedicated user is per month or per year (the follow-up period)</p> <p>Figure 1 presents the number of Rx's per polymedicated user during the follow-up and the analysis is based on the polynomial equation. I ask to what extent this is helpful since the real change happened in the last four months. What happened? A reduction from 30 prescriptions to 12 needs an explanation and discussion, which is missing. A similar decrease is obviously seen in fig. 2 in total costs, which is explained by the fewer prescriptions. This should be discussed.</p> <p>The Y-axis in figure 3 is questionable as it does not include the 0 value, now the seasonal variation in the figure is more dramatic than in reality.</p> <p>The discussion could be condensed and directed on the results and what it means, still appreciating that these are first results and a longer follow-up period may corroborate these results or give hints of new trends. A discussion on which of the drug use indicators are the most relevant would be helpful. The conclusion could be condensed and specifically on the findings. In general, conclusions should give answers to the aims without discussion.</p> <p>A detail on page 9 line 53 – “implantation” or implementation?</p> <p>As mentioned I had problems in understanding whether the analysis is based on administrative data of averages on a population level. Is it possible to follow individual patients and to what extent they are polymedicated through-out the follow-up period. What happens on the individual level? or are all the information based on averages on a monthly basis and no individual longitudinal data is available. In the current manuscript these issues are not clearly stated. This makes the reading of the paper somewhat confusing. By clarifying</p>
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	these issues the manuscript would improve considerably.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Carlos Campillo-Artero

Institution and Country: Balearic Health Service, Palma de Mallorca, Spain

Please state any competing interests or state 'None declared': None

"This is an interesting piece of work that should be welcomed since it is an example of the usefulness that information provided by the evaluations of health services interventions entail with regard to policy making, a health services and policy research goal that has long been called forth in many countries. Having this said notwithstanding the paper should be reviewed in depth before considering its suitability for publication.

My main concerns are fifthfold.

- First, the objective should be reviewed. Strictly speaking, "to analyse drug use indicators..." is not an objective but a methodological step aimed at an end. One analyses indicators in the pursuit of one purpose. This purpose is likely to be the objective. Moreover, in cases such as this one, both process and outcome indicators are what readers and policy makers are interested the most. In this study only process indicators are used. It is worth remembering that what is really at issue and what the study is eventually revolving around is a causal relationship between Rec@t and "process" along with health improvement".

According to the Reviewer suggestion, the purpose of the study has been included, in order to better reflect the aims of the present study:

"The aim of our study was to assess whether electronic prescribing may contribute to rational drug use, particularly in polymedicated patients receiving sixteen or more medications in the public healthcare system in the Barcelona Health Region (BHR). These results will be useful to get prior information for future impact assessment of this technology on risk population."

- "Second, despite the authors recognize some of the limitations of their research, they do not do so explicitly. I would recommend including some paragraphs explicitly devoted to them in the Discussion. Two of these limitations are paramount.

First, there is no control group (what indisputably limits internal validity and undoubtedly impedes establishing causal relationships between Rec@t and both process and outcome indicators)".

Second, as the authors state, the period covered by the study is too short a time to establish these relationships with a reasonable degree of uncertainty, and the implementation of the program is still limited should they actually pursue a complete process and outcome evaluation of the intervention".

Third, the assessment was limited to 6 BHAs. This limitation should be added to the former in order to fully ascertain the full contribution of this paper".

According to the Reviewer suggestion, we have inserted a subheading called "Study limitation" in which we have put limitations explicitly.

- "Fourth, this study is not cross-sectional. It is longitudinal and includes a non-concurrent and a concurrent phase. The authors indicate that it is also descriptive and exploratory. Since this seems to be known ex ante it also precludes from drawing causal associations between Rec@t and the results".

We have changed transversal (cross-sectional) to longitudinal directly in text (Discussion).

- "Fifth, sources of variability of the results are clearly recognized in the Discussion, a fact that further calls for caution before drawing conclusions concerning the "quality, accessibility, safety, efficiency, continuity of care, rational use of drugs ", some of the main features that should be eventually improved with the implementation of a program such as Rec@t. All of them are legitimate goals of the program, but this study does not allow to ascertain to what extent they have been fulfilled".

We agree with the Reviewer, "quality, accessibility, safety, efficiency, continuity of care, rational use of drugs" are the main goals of the electronic prescription system. Our study, as stated in title and aims, focuses in drug use indicators.

- "The study provides a very valuable but initial and partial approach for current managerial, control and follow-up purposes. It is not appropriate though for assessing either the effectiveness, the efficiency or the future impact assessment, given the above mentioned reasons. Both the time elapsed since its inception and its degree of implementation explain among other reasons that the study still falls short of doing so".

We agree with the Reviewer, and as we have indicated the present study should be considered as the first part of an ongoing impact project. Despite the limitations that exist, exploratory and ex ante studies are very useful to get prior information for the design of future studies. In addition, it is crucial in this issue, as it has been shown through a systematic literature review that there is almost no published evidence which can be used as a reference.

Reviewer: 2

Reviewer Name Hannes Enlund

Institution and Country Finnish Medicines Agency, Finland

Please state any competing interests or state 'None declared': None declared

"The increase in costs of pharmaceuticals in different national health service systems has resulted in the need to monitor these costs and assess the effects of different cost containment measures. The manuscript describes efforts in the Catalan Health Service to monitor prescribing in general population and among polymedicated patients using different indicators. Of special interest is the effects of the new e-prescribing system. The manuscript has some merits, but needs to be clarified on certain points especially to an international audience not familiar with the Spanish and Catalan health care system".

- "The introduction is basically a description of the background and Catalan health care and the introduction of a new electronic prescription system. The introduction would improve with a more thorough presentation of the available literature (or lack of it) from an international point of view, especially when the authors have done a systematic literature search".

According to the Reviewer recommendation, the following text has been included in the Introduction, previous to the aim of the study:

"From an international point of view, even though the electronic prescribing system involves a change of paradigm that will enable a better assessment of drug use, there is a lack of evidence reported in the literature in terms of health outcomes evaluation."

- "Some of the current system description could rather be included in the methods section as "Setting" than in the introduction".

Following the Reviewer recommendation, system description that was placed in the Introduction section has now been included to Methods/Setting:

“The Catalan healthcare model is decentralised, to better know the health needs of the population and develop a better relationship with providers in each health region and their respective Basic Health Areas (BHAs). BHAs are the basic territorial units around which primary healthcare services are organised (areas or municipalities), according to the population's access to the services and the efficiency in organising health resources.”

- “The introduction has a paragraph on the aims of the study. This could be reformulated to better reflect the aims, e.g. which drug use indicators and why the study was done or for what purpose the findings will be used. Is the main aim to study the deployment of the e-prescribing or the “effects” in polymedicated patients?”

According to the Reviewer suggestion, the purpose of the study has been included, in order to better reflect the aims of the present study:

“The aim of our study was to assess whether electronic prescribing may contribute to rational drug use, particularly in polymedicated patients receiving sixteen or more medications in the public healthcare system in the Barcelona Health Region (BHR). These results will be useful to get prior information for future impact assessment of this technology on risk population.”

- “The method states that study is interventional, but the discussion states that the study is an exploratory, descriptive and transversal study. This makes the reader somewhat confused as the results is based on a 16 retrospective and 12 month prospective follow-up”.

Following the Reviewer recommendation, we have changed interventional to longitudinal directly in text (Method/Design and setting of the study) and also transversal to longitudinal (Discussion).

- “It would be helpful to give the rationale for using 16 drugs as the cutoff point for “polymedicated” patient since this is not used by other authors”.

The cut-off criterion follows the rationale described in our previous work, which is included here in the References section (Lizano-Díez et al. Profile, cost and pattern of prescriptions for polymedicated patients in Catalonia, Spain. *BMJ Open* 2013; 3(12):e003963).

However, according to the Reviewer suggestion, we have extended the explanation for the cut-off point selected in the study to define polymedicated patients:

“A polymedicated user in the present study was defined as someone receiving 16 or more active principles in a month, according to the Efficiency Indicators in Primary Care that are periodically evaluated by an internal Management Committee in the Catalan Health Service (management level).¹⁸”

- “The polynomial modeling that is used in the figures and appendices I would recommend leaving out. In this case the value of higher order equations is questionable in predicting future trends. Rather analyze the trends of time series for period 1 (before) and period 2 (after) and possible interactions”.

Following the Reviewer recommendation, we have leaving out polynomial modeling and instead of it we have analyze the trends of time series in each figure.

- “For an international audience some additional information would be helpful for better understanding of the setting and system. For example for a how long time period is a prescription usually issued in chronic diseases, one month, three months or a year? What is the average number of prescriptions per capita/year or month in Catalan or Barcelona health region and also cost per prescription”.

In order to better understand the setting and system, as the Reviewer suggests, we have included the following paragraph in Methods/Setting and /Data source, respectively:

(Methods/Setting) "In terms of prescriptions billing, during the period 2008-2010, the average of total prescriptions per year in Catalonia was $143,753,915 \pm 4,500,218$ ($99,786,576 \pm 1,251,654$ in BHR). According to the average yearly number of prescriptions per capita and cost per prescription, both indicators were similar in Catalonia and BHR: 18.98 ± 0.50 vs. 18.94 ± 0.78 and 13.24 ± 0.18 vs. 13.25 ± 0.19 respectively".

(Data source) "Prescriptions in paper format are usually issued for 3 months ("chronic patients program" in primary care setting) and electronic prescriptions are usually issued for 12 months (maximum); at least once a year patients visit the doctor to renew them."

- "I had also problems in trying to understand whether the same person can be a polymedicated patient in different points of the follow-up and what the consequences are for the analysis. Is there a real increase in polymedicated patients (new polymedicated or the same patients as before?). Is the analysis based on prescriptions or individuals counted only once during the follow-up?"

Following the Reviewer recommendation, we have included a wide explanation about the size of polymedicated population in Methods/Data source and Results, respectively:

(Methods/Data source) "Polymedicated users were selected monthly, so polymedicated population varied throughout the whole study (28 months, which involved 28 data analysis). Due to the fact that each user has its own identification code, given by the personal healthcare card, subsequent analyses could be carried out so as to determine monthly duplicities of users."

(Results) "1,575 polymedicated users were analyzed; 54.4% of them were only polymedicated in 1 month of the study and 4% of them had that condition in > 10 months; there were no users being polymedicated during > 20 months."

In addition, in order to clarify calculations, we have included a brief explanation in each Table:

* In general population (Table 1): "Results were calculated from global cumulative data in each BHA." Thus, results are not presented as an average + standard deviation.

* In polymedicated users (Table 2): "Averages of monthly global data in the 6 BHAs were calculated for prescriptions/user, cost/user and cost/prescription".

Following this rationale, the average number of prescriptions per polymedicated user was calculated as follows (i.e. in BHA1): (Mean number of monthly prescriptions per user in BHA1) + (Standard deviation of number of monthly prescriptions per user in BHA1)

- "The results section would improve by inserting subheadings on the deployment in general population and on the other hand results related to "polymedicated" patients".

Following the Reviewer recommendation, we have included these subheadings directly in text.

- "On page 6 line 10 says "only 6 reached the highest cumulative implementation grade..." rather say "only 6 reached a 25% implementation grade. Then the next sentence can be deleted".

Following the Reviewer recommendation, we have included this change directly in text.

- "In Table 1 insert a column on average number of prescriptions/user in the different BHAs (i.e. $438,228/107,306=4.1$ etc.)"

Following the Reviewer recommendation, we have included this column directly in Table 1.

- "Table 2 says "number of polymedicated users" but there is no such number included! It is also unclear whether average number of prescriptions per polymedicated user is per month or per year (the follow-up period)"

Following the Reviewer recommendation, we have changed the title of Table 2 directly in the text and we have also included the following sentence to clarify the table's content: "All data included make

reference to the whole prospective follow-up period (average data resulting from 12 months, post-implementation period).”

- “Figure 1 presents the number of Rx's per polymedicated user during the follow-up and the analysis is based on the polynomial equation. I ask to what extent this is helpful since the real change happened in the last four months. What happened? A reduction from 30 prescriptions to 12 needs an explanation and discussion, which is missing. A similar decrease is obviously seen in fig. 2 in total costs, which is explained by the fewer prescriptions. This should be discussed”.

Taking into account the Reviewer comment, we realized that there was a mistake in the Figures 1 and 2. We have corrected in the corrected version of the manuscript.

- The Y-axis in figure 3 is questionable as it does not include the 0 value, now the seasonal variation in the figure is more dramatic than in reality.

Following the Reviewer recommendation we have changed values on the y-axis of the figure.

- “The discussion could be condensed and directed on the results and what it means, still appreciating that these are first results and a longer follow-up period may corroborate these results or give hints of new trends. A discussion on which of the drug use indicators are the most relevant would be helpful. The conclusion could be condensed and specifically on the findings. In general, conclusions should give answers to the aims without discussion”.

Taking into account the Reviewer comments we have tried to condense discussion and also conclusion.

- “A detail on page 9 line 53 – “implantation” or implementation?”

We wanted to say: Implementation. We have included this change directly in text.

- “As mentioned I had problems in understanding whether the analysis is based on administrative data of averages on a population level. Is it possible to follow individual patients and to what extent they are polymedicated through-out the follow-up period. What happens on the individual level? Or are all the information based on averages on a monthly basis and no individual longitudinal data is available. In the current manuscript these issues are not clearly stated. This makes the reading of the paper somewhat confusing. By clarifying these issues the manuscript would improve considerably”.

We have answered to this general comment in the previous answers to the Reviewer comment.

VERSION 2 – REVIEW

REVIEWER	Carlos Campillo-Artero' Balearic Health Service, Spalin
REVIEW RETURNED	23-Sep-2014

GENERAL COMMENTS	After having gone over this revised manuscript, I think it should be accepted for publication in its current form.
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REVIEWER	Hannes Enlund Finnish Medicines Agency
REVIEW RETURNED	25-Sep-2014

GENERAL COMMENTS	<p>The paper has been adequately corrected and can be accepted. I would recommend to rephrase the conclusions. I dont think you can say that "drug use indicators decreased in polymedicated patients" either you have say "number of prescriptions and costs decreased" or what I would prefer "The rationality of prescribing in polymedicated patients improved." There is a typo on page 9 line 28 "used" should be "user"</p> <p>Rephrase conclusions e.g. "Results suggest that after the implementation of electronic prescribing the rationality of presribing in polymedicated patients improved." In addition.....</p> <p>correct typo on page 9 line 28 "used" should be "user"</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name Carlos Campillo-Artero

Institution and Country Balearic Health Service, Spain

Please state any competing interests or state 'None declared': None

- "After having gone over this revised manuscript, I think it should be accepted for publication in its current form"

Reviewer: 2

Reviewer Name Hannes Enlund

Institution and Country Finnish Medicines Agency

Please state any competing interests or state 'None declared': "None declared"

"The paper has been adequately corrected and can be accepted.

I would recommend to rephrase the conclusions.

I dont think you can say that "drug use indicators decreased in polymedicated patients" either you have say "number of prescriptions and costs decreased" or what I would prefer "The rationality of prescribing in polymedicated patients improved. There is a typo on page 9 line 28 "used" should be "user"

- Rephrase conclusions e.g. "Results suggest that after the implementation of electronic prescribing the rationality of prescribing in polymedicated patients improved."

According to the Reviewer comment, we have modified conclusions including the recommended sentence directly in the manuscript.

- In addition..... correct typo on page 9 line 28 "used" should be "user"

Following the Reviewer recommendation, we have corrected the word directly in the manuscript